Drug Safety Update

MHRA

Latest advice for medicines users

The monthly newsletter from the Medicines and Healthcare products Regulatory Agency and its independent advisor the Commission on Human Medicines

Volume 14 Issue 2 September 2020

Contents

The Medicines and Healthcare products Regulatory Agency (MHRA) is the government agency responsible for ensuring that medicines and medical devices work and are acceptably safe.

The Commission on Human Medicines gives independent advice to ministers about the safety, quality, and efficacy of medicines. The Commission is supported in its work by Expert Advisory Groups that cover various therapeutic areas of medicine.

NICE accredited
www.nice.org.uk/accreditation

MHRA is accredited by NICE to provide Drug Safety Update. Further information can be found on the NICE Evidence Search portal: www.evidence.nhs.uk/

To subscribe to monthly email alerts of Drug Safety Update see: https://www.gov.uk/government/organisations/medicines-and-healthcare-products-regulatory-agency/email-signup

First, we communicate important recommendations for opioid medicines (opioids) following a review of the risks of addiction and dependence associated with prolonged use of opioids for non-cancer pain (page 2). Before prescribing opioids, discuss with the patient the risks and features of tolerance, dependence, and addiction, and agree together a treatment strategy and plan for the end of treatment.

See also page 5 for the recommendation from the UK's Commission on Human Medicines (CHM) that fentanyl transdermal patches are contraindicated in opioid-naive patients in the UK.

Next, prescribers and dispensers of once-weekly methotrexate for autoimmune diseases are advised of new measures to reduce the risk of potentially fatal overdoses following inadvertent more frequent dosing (including daily administration). See page 7 for the advice.

On page 10, we advise of the risk of cutaneous amyloidosis at insulin injection sites and the impact that repeatedly administering insulin into affected sites can have on glycaemic control.

Opioids: risk of dependence and addiction

New recommendations following a review of the risks of dependence and addiction associated with prolonged use of opioid medicines (opioids) for non-cancer pain.

Before prescribing opioids, discuss with the patient the risks and features of tolerance, dependence, and addiction, and agree together a treatment strategy and plan for end of treatment.

Advice for healthcare professionals:

- opioid medicines (opioids) provide relief from serious short-term pain; however long-term use in non-cancer pain (longer than 3 months) carries an increased risk of dependence and addiction
- discuss with patients that prolonged use of opioids may lead to drug dependence and addiction, even at therapeutic doses – warnings have been added to the labels (packaging) of UK opioid medicines to support patient awareness
- before starting treatment with opioids, agree with the patient a treatment strategy and plan for end of treatment
- explain the risks of tolerance and potentially fatal unintentional overdose, and counsel patients and caregivers on signs and symptoms of opioid overdose to be aware of (see opioids safety information leaflet)
- provide regular monitoring and support especially to individuals at increased risk, such as those with current or past history of substance use disorder (including alcohol misuse) or mental health disorder
- at the end of treatment, taper dosage slowly to reduce the risk of withdrawal effects associated with sudden cessation of opioids; tapering from a high dose may take weeks or months
- consider the possibility of hyperalgesia if a patient on long-term opioid therapy presents with increased sensitivity to pain
- consult the latest advice and warnings for opioids during pregnancy in the product information and in clinical resources
- report suspected dependence or addiction to any medicine, including to an opioid, via the Yellow Card scheme

National review of benefits and risks of opioid medicines

More than 20 different opioid medicines (opioids) are authorised for use in the treatment of pain in the UK. The relative potency differs between these medicines. Opioids relieve pain but may not remove pain altogether.

Considerable concern has been raised regarding prescribing rates of opioids in the UK and the awareness of healthcare professionals and patients of the risks of dependence and addiction. This includes Public Health England's evidence review of dependence and withdrawal associated with some prescribed medicines.

In 2019, the Commission on Human Medicines (CHM) convened an Expert Working Group to examine the benefits and risks of opioids in the relief of non-cancer pain, including information available to healthcare professionals and patients about the risks of dependence and addiction. Following this review, CHM has made recommendations to improve information for prescribers and patients about these risks to protect public health.

To make it clear that a medicine contains an opioid and that there is a risk of addiction (a recognised term by patients) with prolonged use, CHM recommended that the packaging for all opioid medicines in the UK carries the warnings 'Can cause addiction' and 'Contains opioid'. The CHM also recommended including further information on the risk of tolerance, dependence and addiction in the product information.

The changes apply to the following opioids:

Alfentanil	Dihydrocodeine	Meptazinol	Oxycodone	Remifentanil
Buprenorphine	Dipipanone	Methadone	Papaveretum	Tapentadol
Codeine	Fentanyl	Morphine	Pentazocine	Tramadol
Diamorphine	Hydromorphone	Opium	Pethidine	

Tolerance, dependence, and addiction

Product information for opioids in the UK will include consistent warnings of the risks of tolerance and dependence and addiction. Patients may find that treatment is less effective with long-term use and express a need to increase the dose to obtain the same level of pain control as initially experienced. This could indicate that the patient is developing tolerance and dependence.

For all patients, prolonged use of opioids may lead to drug dependence (and in some patients addiction/opioid use disorder), even at therapeutic doses (see resources from the Faculty of Pain Medicine). The risks are increased in individuals with current or past history of substance use disorder (including alcohol misuse) or mental health disorder (for example, major depression). Additional support and monitoring may be necessary when prescribing for patients at risk of opioid misuse.

Typical signs of addiction are:

- Expression of craving for the drug, even if it is causing adverse effects on overall health
- Expression of a need for more, or reporting additional use of other pain-relief medicines
- Taking medicines for reasons other than pain relief
- Experiencing withdrawal side effects when opioids are stopped suddenly

Withdrawal reactions

Dependence and addiction to opioids are associated with adverse reactions of withdrawal upon sudden cessation of treatment that make it harder to stop taking these medicines. CHM has therefore recommended that before prescribing an opioid a discussion should be held with the patient, to put in place a withdrawal strategy for ending treatment with their opioid medicine.

Withdrawal from an opioid is characterised by shivers, diarrhoea, difficulty sleeping (insomnia), sweating, body aches (myalgia), widespread or increased pain, irritability and agitation, and nausea and vomiting. Other signs and symptoms include restlessness, lacrimation, rhinorrhoea, yawning, mydriasis, palpitations, anxiety, hyperkinesia, tremor, weakness, anorexia, abdominal cramps, and increased blood pressure, respiratory rate, and heart rate.

Tapering doses

To minimise the risk of withdrawal reactions, the dose of opioid should be tapered slowly at the end of treatment. This can take weeks or months, depending on individual response and the dose taken. Healthcare professionals should advise patients not to stop suddenly taking their medicines or try to self-medicate to overcome withdrawal effects. Self-medication with opioids can result in overdose and potentially death.

Hyperalgesia

Some patients can develop hyperalgesia (increased sensitivity to pain) with long-term use of opioids. This might be qualitatively and anatomically distinct from pain related to disease progression or to breakthrough pain resulting from development of opioid tolerance. These symptoms may resolve with a gradual reduction in opioid dose.

Opioids in pregnancy

Opioids readily cross the placenta, therefore if used during pregnancy neonates may become dependent and experience neonatal abstinence syndrome at birth. Extra vigilance is required and appropriate treatment should be made available.

Resources for prescribers and dispensers

We have developed an opioids safety information leaflet on the risks of dependence and addiction (available online plus as a PDF leaflet). This advice for patients and their families and carers was developed following consultation with a number of stakeholder organisations, charities, and patient groups. We encourage healthcare professionals to use this information alongside the statutory patient information leaflet supplied with opioid medicines.

Additional guidance is available for healthcare professionals and patients at the following websites:

- Opioids Aware – Faculty of Pain Medicine at the Royal College of Anaesthesiologists
- Management of chronic pain – Scottish Intercollegiate Guidelines Network (SIGN)

Report side effects, including dependence

If a patient experiences any side effect related to dependence to a medicine or is recognised by the prescriber to be dependent, CHM encourages prescribers, patients, or carers to report this to the MHRA through the Yellow Card scheme with the term ‘dependence’. Use of this specific term will assist the MHRA to monitor the rates reported in the UK and therefore to further protect public health.

Any other suspected adverse drug reactions associated with opioids should also be reported to the MHRA through the Yellow Card scheme. Report via the Yellow Card website, Yellow Card App (download at iTunes Yellow Card for iOS devices or at PlayStore Yellow Card for Android devices), or some clinical IT systems (EMIS/SystmOne/Vision/MiDatabank).

Article citation: Drug Safety Update volume 14, issue 2: September 2020: 1.

Transdermal fentanyl patches for non-cancer pain: do not use in opioid-naive patients

Following a review of the risks associated with use of opioid medicines for non-cancer pain, the Commission on Human Medicines (CHM) has recommended that fentanyl transdermal patches are contraindicated in opioid-naive patients in the UK.

Advice for healthcare professionals:

- Fentanyl is a potent opioid – a 12 microgram (µg) per hour fentanyl patch equates to daily doses of oral morphine of up to 45mg a day
- do not use fentanyl patches in opioid-naive patients
- use other analgesics and other opioid medicines (opioids) for non-cancer pain before prescribing fentanyl patches
- if prescribing fentanyl patches, remind patients of the importance of:
    - not exceeding the prescribed dose
    - following the correct frequency of patch application, avoiding touching the adhesive side of patches, and washing hands after application
    - not cutting patches and avoiding exposure of patches to heat including via hot water (bath, shower)
    - ensuring that old patches are removed before applying a new one
    - following instructions for safe storage and properly disposing of used patches or patches that are not needed (see advice issued previously); it is particularly important to keep patches out of sight and reach of children at all times
- make patients and caregivers aware of the signs and symptoms of fentanyl overdose and advise them to seek medical attention immediately (by dialling 999 and requesting an ambulance) if overdose is suspected
- remind patients that long-term use of opioids in non-cancer pain (longer than 3 months) carries an increased risk of dependence and addiction, even at therapeutic doses (see Drug Safety Update on risk of dependence and addiction with opioids); before starting treatment with opioids, agree with the patient a treatment strategy and plan for end of treatment
- report suspected adverse drug reactions, including dependence, accidental exposure, or overdose associated with fentanyl patches, via the Yellow Card scheme

Review of opioid medicines

Considerable concern has been raised regarding the prescribing of opioids in the UK (see Drug Safety Update on risk of dependence and addiction with opioids). In 2019, the Commission on Human Medicines (CHM) convened an Expert Working Group to examine the benefits and risks of opioids in the relief of non-cancer pain.

During this review it was noted that there have been reports of serious harm, including fatalities, associated with fentanyl patches in both opioid-naive patients and opioid-experienced patients.

Up to May 2020, we have received 13 Yellow Card reports in which opioid-naive patients have experienced respiratory depression following use of fentanyl and additional Yellow Card reports in which respiratory depression was reported in patients switched from another opioid to an inappropriately high dose of fentanyl. There was no evidence of intentional overdose in these cases.

There is considerable risk of respiratory depression with the use of fentanyl especially in opioid-naive patients. There is also significant risk with too rapid an escalation of dose, even in long-term opioid users.

Fentanyl is a potent opioid analgesic – a 12 microgram (µg) per hour fentanyl patch equates to daily doses of oral morphine of up to 45mg a day. Because of the risk of significant respiratory depression, in non-cancer patients fentanyl patches should only be used in those who have previously tolerated opioids. CHM has recommended a strengthening of the current warnings and a contraindication for use in opioid-naive patients in the UK for non-cancer pain.

The initial dose of fentanyl should be based on a patient's opioid history. Please consult the Summaries of Product Characteristics (SmPC) for each medicine for information on starting doses and dose conversion. Prescribers should take into account the morphine equivalence of fentanyl (see morphine equivalence table in SmPCs and from the Faculty of Pain Management).

Advice for patients

On the advice of CHM, the patient information leaflet (PIL) for fentanyl patches has been updated with harmonised headline information regarding their safe use. Please direct both new and current users of fentanyl patches to the updated PIL.

Accidental exposure to transdermal fentanyl can occur if a patch is swallowed or transferred to another individual (see Drug Safety Update, September 2008, and Drug Safety Update, July 2014). In 2014, following a European review, advice on minimising risk of accidental transfer was added to both the SmPC and the PIL for transdermal fentanyl products. In October 2018, following further reports of deaths by accidental transfer of patches, the MHRA published patient advice (large print version). This can still be used as a resource when discussing with patients how to use and dispose of fentanyl patches safely.

Report to the Yellow Card scheme

Please report medication errors resulting in harm, including overdose and accidental exposure to a medicine, or any other suspected side effects on a Yellow Card. If a patient experiences any side effect related to dependence or is recognised by the prescriber to be dependent, CHM encourages prescribers, patients, or carers to report this to the MHRA through the Yellow Card scheme with the term 'dependence'. Use of this specific term will assist the MHRA to monitor further the rates reported in the UK and therefore to further protect public health.

Your report helps to improve the safety of medicines in the UK. Report via the Yellow Card website, Yellow Card App (download at iTunes Yellow Card for iOS devices or at PlayStore Yellow Card for Android devices), or some clinical IT systems (EMIS/SystmOne/Vision/MiDatabank).

Article citation: Drug Safety Update volume 14, issue 2: September 2020: 2.

Methotrexate once-weekly for autoimmune diseases: new measures to reduce risk of fatal overdose due to inadvertent daily instead of weekly dosing

In autoimmune conditions and some cancer therapies, methotrexate should be taken only **once a week;** however, we continue to receive reports of inadvertent overdose due to more frequent dosing (including daily administration). New measures have been implemented to prompt healthcare professionals to record the day of the week for intake and to remind patients of the dosing schedule and the risks of overdose.

Advice for healthcare professionals:

Advice for prescribers:

- before prescribing methotrexate, make sure that the patient is able to understand and comply with once-weekly dosing
- consider the patient's overall polypharmacy burden when deciding which formulation prescribe, especially for a patient with a high pill burden
- decide with the patient which day of the week they will take their methotrexate and note this day down in full on the prescription
- inform the patient and their caregivers of the potentially fatal risk of accidental overdose if methotrexate is taken more frequently than once a week; specifically, that it should not be taken daily
- advise patients of the need to promptly seek medical advice if they think they have taken too much

Advice for dispensers:

- remind the patient of the once-weekly dosing and risks of potentially fatal overdose if they take more than has been directed
- where applicable, write the day of the week for intake in full in the space provided on the outer package
- demonstrate the Patient Card included with the methotrexate packet and encourage patients to:
    - write the day of the week for intake on the patient card
    - carry it with them to alert any healthcare professionals they consult who are not familiar with their methotrexate treatment about their dosing schedule (for example, on hospital admission, change of care)

Review of medication errors with once-weekly methotrexate

In autoimmune conditions (and less commonly, in some cancer therapy regimens), methotrexate should be taken **once a week**.

Measures (including a patient safety alert in 2006) have previously been put in place to minimise the risk of inadvertent overdose due to more frequent dosing of methotrexate, however a small number of reports continue to be received.

Since 1 Jan 2006 and up to 30 July 2020, we are aware of 11 Yellow Card reports of serious toxicity associated with inadvertent daily dosing of once-weekly methotrexate in the UK, with 4 of these serious reports received since January 2016.

Overdose of methotrexate can lead to serious adverse effects such as haematopoietic disorders (leukopenia, thrombocytopenia, anaemia, and pancytopenia) and gastrointestinal reactions (mucositis, stomatitis, oral ulceration, gastrointestinal ulceration, and gastrointestinal bleeding). Some reports of overdose have been fatal. In these fatal cases, events such as sepsis or septic shock, renal failure, and aplastic anaemia were reported.

A European review of these types of medication error has looked at the root causes of these errors and set out several recommendations to minimise the likelihood of them occurring. A letter has been sent to prescribers and pharmacists involved in provision of methotrexate for autoimmune diseases.

Key recommendations

Prescribing advice

Medication errors that lead to taking more than the intended dose (including daily instead of once-weekly dosing) have been identified at all steps in the treatment pathway, including prescribing and dispensing of methotrexate, transfer of care (for example, hospital admission and discharge), and communicating with patients.

Methotrexate should only be prescribed by healthcare professionals who are fully aware of the benefits and risks of treatment and who have all necessary prescribing competence.

Healthcare professionals should take into consideration a patient's overall polypharmacy burden when prescribing an oral formulation once-weekly and ensure that the patient is able to comply with once-weekly dosing when prescribing methotrexate. They should inform patients of the risks associated with taking methotrexate more frequently than prescribed, and specifically, that it should not be taken daily.

Patients should be advised to seek urgent medical attention if they think they have taken too much methotrexate.

Changes to the instructions and packs

The product information and outer and inner packaging of all methotrexate products for once-weekly dosing will carry a warning about the dosing schedule and the consequences of dosing errors.

The outer package warning will also include a space for the dispenser to write the day of the week for intake. Advice on dividing the once-weekly dose is being removed from the product information since this was identified as a source of confusion that could lead to medication error.

For methotrexate tablets, availability in bottle and tube packaging will be phased out over a period of 4 years.

Patient card and educational materials

Oral methotrexate products with indications requiring once-weekly dosing will come with a patient card (July 2020), which will prompt patients to take methotrexate once a week and to record the day of the week for intake. It will also help patients to identify the signs and symptoms of overdose.

Instruct patients to carry the card with them in their purse or wallet and to use it to alert any healthcare professionals they consult who are not familiar with their methotrexate treatment about their once-weekly dosing schedule (for example, on hospital admission, change of care). Educational materials (July 2020) for healthcare professionals will also be made available for oral products with indications requiring once-weekly dosing. These materials should be used in conjunction with local guidance materials if available.

Background

Methotrexate is authorised for two different therapeutic areas, each of them with a different administration schedule:

- For the treatment of cancer in which regimens vary and can require daily administration of methotrexate
- For the treatment of autoimmune diseases including rheumatoid arthritis, psoriasis, and Crohn's disease, which require **once-weekly use**

Report on a Yellow Card

Suspected adverse reactions and any medication error that results in patient harm should be reported to the MHRA through the Yellow Card scheme.

You can report suspected side effects electronically via:

- the Yellow Card website
- the free Yellow Card app; download from iTunes Yellow Card for iOS devices or PlayStore Yellow Card for Android devices
- some clinical IT systems (EMIS/SystmOne/Vision/MiDatabank) for healthcare professionals

Article citation: Drug Safety Update volume 14, issue 2: September 2020: 3.

Insulins (all types): risk of cutaneous amyloidosis at injection site

Cutaneous amyloidosis at the injection site has been reported in patients using insulin and this may affect glycaemic control. Remind patients to rotate injection sites within the same body region.

Advice for healthcare professionals:

- injection of insulin (all types) can lead to deposits of amyloid protein under the skin (cutaneous amyloidosis) at the injection site
- cutaneous amyloidosis interferes with insulin absorption, and administration of insulin at an affected site can affect glycaemic control
- remind patients to rotate injection sites within the same body region to reduce or prevent the risk of cutaneous amyloidosis and other skin reactions (for example, lipodystrophy)
- consider cutaneous amyloidosis as a differential diagnosis to lipodystrophy when a patient presents with subcutaneous lumps at an insulin injection site
- advise patients:
    - that insulin may not work very well if they inject into an affected 'lumpy' area
    - to contact their doctor if they are currently injecting insulin into a 'lumpy' area before changing injection site since a sudden change may result in hypoglycaemia
    - to monitor carefully blood glucose after a change in injection site and that dose adjustment of insulin or other antidiabetic medication may be needed
- report serious adverse drug reactions associated with insulin to the Yellow Card Scheme

European review of cutaneous amyloidosis

Insulin is used to treat all types of diabetes (including type 1 diabetes, type 2 diabetes and gestational diabetes). Patients who self-inject insulin are already advised to rotate injections within one area, and change injection sites completely every week or two (for example, from the abdomen to thigh), and to be aware that the injection site will affect blood sugar levels.

A recent European review of reports of insulin-derived cutaneous amyloidosis at insulin injection sites concluded that there is a clear causal relationship between cutaneous amyloidosis and all insulins and insulin-containing products.

The Summaries of Product Characteristics and Patient Information Leaflets for all insulins and insulin-containing products are being updated to include this risk. Advice will also make clear the importance of site rotation and careful blood glucose monitoring following change of injection site to an unaffected area.

Characteristics of cutaneous amyloidosis

Insulin-derived amyloidosis is a specific form of localised cutaneous amyloidosis composed of insulin fibrils. It is likely caused by insulin accumulation at the injection sites, especially if these sites are used for repeated subcutaneous injections.

The European review considered cases of insulin-derived cutaneous amyloidosis reported in patients treated with all types of insulin. Some were identified by either histological examination, computerised tomography, or a combination of these. Presence of insulin in the amyloid was recognised by immunohistochemical analysis and in a single case further validated by mass spectrometry.

In many of the cases initially analysed of the review, this resulted in poor glycaemic control (hyperglycaemia and hypoglycaemia).

The evidence showed in many cases patients were routinely injecting into the same sites repeatedly rather than rotating injection sites. When outcome of glycaemic control was reported, most patients recovered after they began to use a proper site-rotation technique.

In the UK, up until the end of July 2019, 2 reports of cutaneous amyloidosis in patients receiving insulin therapy have been received via the MHRA's Yellow Card Scheme.

The European review was not able to estimate the frequency of cutaneous amyloidosis in patients using insulin from the data available, but reports have been received only very rarely. The literature suggests that cases of cutaneous amyloidosis may be under-reported and misdiagnosed as lipohypertrophy (a common increase in fat cells due to growth factor effect of insulin). Both conditions are characterised by lumps in the skin. However, where lipohypertrophy lesions are lobular and regress after stopping insulin injection, amyloid lesions are more solid and firm, do not regress quickly, and usually require surgical excision to treat.

While amyloid lesions can delay insulin absorption and affect glycaemic control if used as a site for administration, the skin changes are thought to be localised. Although some cases of cutaneous amyloidosis were reported as of a serious nature, they were mostly reported as such due to hospital admission to resect amyloid lesion. Aside from impact on glycaemic control, no other complications have been recognised.

Recommendations for reducing the risk of cutaneous amyloidosis

Patients who inject insulin at the same site regularly are at an increased risk of developing cutaneous amyloidosis at the injection site and consequently may have poor diabetes control due to lack of insulin absorption due to the amyloid mass. To prevent or reduce this, patients should be advised to rotate injection sites within the same body region.

There is a risk of hypoglycaemia in patients that suddenly change injection site from an area with cutaneous amyloidosis to an unaffected area (for example, changing the injection site from the torso to the leg). Patients should therefore carefully monitor blood glucose after changing injection site and consider adjusting the dose of insulin or antidiabetic medication to avoid hypoglycaemia, as needed.

Report on a Yellow Card

Please continue to report suspected adverse drug reactions (ADRs) on a Yellow Card. Reporting suspected ADRs, even those known to occur in association with the medicine, adds to knowledge about the frequency and severity of these reactions and can be used to identify patients who are most at risk. Your report helps the safer use of medicines.

Healthcare professionals, patients, and caregivers are asked to submit reports using the Yellow Card scheme electronically using:

- the Yellow Card website
- the Yellow Card app; download from iTunes Yellow Card for iOS devices or PlayStore Yellow Card for Android devices
- some clinical IT systems (EMIS/SystmOne/Vision/MiDatabank)

When reporting please provide as much information as possible, including information about medical history, any concomitant medication, onset, treatment dates, and product brand name.

Article citation: Drug Safety Update volume 14, issue 2: September 2020: 4.

Letters and drug alerts sent to healthcare professionals in August 2020

Letters

In August 2020, the following letters were sent or provided to relevant healthcare professionals:

- RoActemra (tocilizumab) 162 mg Solution for Injection in Pre-filled Syringe: Interim supply of Irish livery stock to mitigate supply disruption
-
- Fresenius Propoven 2% Emulsion for Injection or Infusion (propofol): Interim Supply of European Stock to Mitigate Supply Disruption
-
- Wockhardt UK's Amoxicillin Sodium 250mg, 500mg and 1g powder for solution for injection: caution and monitoring requirements

So far in September 2020, the following has been provided to healthcare professionals to support the supply of medicines:

- Ativan 4mg/ml Solution for Injection (Lorazepam): Temporary supply of a different presentation and changes to the instructions

Drug alerts

Class 2 Medicines Recall: Pharmaram Ltd, Clexane 4,000 IU (40mg)/0.4ml Syringes, EL (20)A/37. Issued 4 August 2020. A specific batch of Clexane 4,000IU (40mg)/0.4ml syringes has an error on the labelling affixed to the plastic blister packaging encasing the syringe (the label incorrectly states 'Clexane 6,000IU (60mg)/0.6ml Syringes'). Stop supplying the products immediately and return to supplier. Inform patients who have been supplied this batch that the error is only with the labelling on the plastic blister packaging encasing the syringe.

Class 2 Medicines Recall: Huddersfield Pharmacy Specials MS 19055, Phosphates Solution for Infusion 500ml, EL (20)A/38. Issued 10 August 2020. The listed batches of phosphates solution for infusion have been recalled due to observation of precipitation in one batch. Stop supplying the products immediately and return to supplier.

Class 2 Medicines Recall: Sanofi Fasturtec 7.5 mg, 1.5 mg/ml powder and solvent for concentrate for solution for infusion, EL (20)A/40. Issued 24 August 2020. Batch number A9306 has been recalled as a precautionary measure due to an out of specification result. Stop supplying the products immediately and return to supplier.

Class 3 Medicines Recall: Accord-UK Ltd, Digoxin Tablets BP 250 micrograms, EL (20)A/35. Issued 3 August 2020. There is an issue related to decommissioning of a specific batch. Although there is no risk to product quality, any remaining stock should be quarantined and returned.

Class 4 Medicines Defect Information: Crescent Pharma Ltd, SyreniRing 0.120 mg/0.015 mg per 24 hours, vaginal delivery system, EL (20)A/36. Issued 3 August 2020. The Patient Information Leaflet (PIL) within the packs for the listed batches are missing important safety relevant text changes. If dispensing any of the listed batches, ensure patients are aware of any missing information.

Class 4 Medicines Defect Information: SmofKabiven extra Nitrogen Electrolyte Free, EL (20)A/39, PL 08828/0269. Issued 13 August 2020. There is an error on the bag labels for SmofKabiven extra nitrogen electrolyte free emulsion for infusion. Healthcare professionals should be aware that there is a product available with electrolytes and caution should be exercised when dispensing and administering this product.

Article citation: Drug Safety Update volume 14, issue 2: September 2020: 5.